Cryotherapy for Cosmetic Procedures

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Abstract

Cryosurgery or cryotherapy is a surgical method that consists of application of very low temperatures to living tissue, resulting in cell destruction. It is considered a versatile treatment option for benign and malignant lesions, with rapid delivery, low cost, and lower morbidity than regular surgery. Cryotherapy may be used to treat a wide range of skin conditions, and in clinical practice, it is most commonly used for treating actinic keratoses, seborrheic keratoses, and verrucae.

Keywords

Cryotherapy • Dermatology • Dermatologic surgery • Benign lesions • Malignant lesions • Actinic keratoses • Seborrheic keratosis

Contents

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Introduction

Cryosurgery or cryotherapy is a surgical method that consists of application of very low temperatures to living tissue, resulting in cell destruction (Pasquali et al. 2010). Various methods for freezing skin lesions have been described, such as salt-ice mixture, carbon dioxide snow, nitrous oxide, dimethyl ether, and propane, but liquid nitrogen works faster and achieves much lower temperatures (−196 °C) (Kuflik and Kuflik 2012; Lawrence and Tefler 2010; Vujewich and Goldberg 2008). It is also easy to store and non-flammable (Vujewich and Goldberg 2008).

Cryosurgery is considered a versatile treatment option for benign and malignant lesions, with rapid delivery, low cost, and lower morbidity than regular surgery. It is more acceptable in elderly patients with comorbidities and pregnant women. It also has good aesthetic results, and it can be performed either in surgical areas or doctor's offices (Pasquali et al. 2010). It is useful as a primary

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or an alternate form of treatment (Kuflik and Kuflik 2012).

Cryotherapy may be used to treat a wide range of skin conditions. In the USA, cryosurgery is most commonly used for treating actinic keratoses, seborrheic keratoses, and verrucae (Farhangian et al. 2015; Afsar et al. 2015). In this chapter we will only discuss benign lesions that may cause aesthetic impairment to the patient and premalignant lesions.

Basic Principles

The aim of cryosurgery is to promote freezing of the tissue with subzero temperatures, resulting in tissue damage and subsequent healing by second intention (Pasquali et al. 2010) (Fig. 1). This process leads to cellular structural changes resulting in cell death that occurs due to:

- Cell injury with water crystalizing outside the cell. Initially, water moves out of the cell by osmosis, causing internal dehydration and cell damage. Freezing causes internal crystal formation and further cell disruption. The thawing process leads to larger crystal formation The more freeze-thaw cycles, the longer the thawing time; the coldest the temperature, the greater the cell damage (Pasquali et al. 2010; Kuflik and Kuflik 2012).
- Vasoconstriction, blood stasis, and anoxia. Free radical formation after compensatory vasodilatation contributes to the cell damage (Pasquali et al. 2010; Kuflik and Kuflik 2012; Vujewich and Goldberg 2008).
- Immunologic effect: Release of antigenic components – controversial in the current literature (Pasquali et al. 2010; Lawrence and Tefler 2010).
- pH changes (Kuflik and Kuflik 2012).
- Impairment of homeostatic functions (Kuflik and Kuflik 2012).

The ideal treatment is considered repeated freeze-thaw cycles, rapid freezing, and slow thawing (the thaw time is usually two or three times longer than the freeze time) (Kuflik and Kuflik 2012; Lawrence and Tefler 2010).

Necrosis usually occurs at the center of the area of application, where the temperature should range between −30 °C and −40 °C. There is a rim of partially damaged tissue, and in the peripheral areas, some cells remain alive, but with such injury that triggers later apoptosis. Thermocouples inside the lesion or electrodes around can help to monitor the temperature (Pasquali et al. 2010; Kuflik and Kuflik 2012), but their placement is difficult to standardize (Petres et al. 1996). In practice, the temperature does not need to be measured because clinical studies suggest determined duration of freezing times for the most common skin lesions (Lawrence and Tefler 2010).

The lateral spread of freeze is also important and refers to the freezing of the tissue beyond the margins of the lesion. Benign lesions require usually 2–3 mm, and malignant lesions such as basal or squamous cell carcinomas should reach at least 3–5 mm, or more, if possible (Kuflik and Kuflik 2012).

Melanocytes are the most sensitive to freeze, with cell destruction at −4 °C to −7 °C (depigmentation may occur, especially in more pigmented

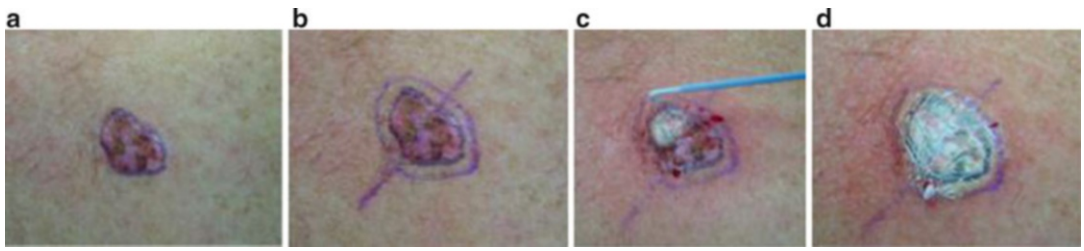

Fig. 1 Basal Cell carcinoma treated by open spray technique. In lager lesions,it is necessary to divide into smaller zones to promote more effective freezing and thawing cycles

Fig. 2 Hypopigmentation after cryotherapy with liquid nitrogen for actinic keratosis treatment on the trunk

patients). Keratinocyte death requires −20 to −30 °C. Fibroblasts are more resistant to freeze and require temperatures ranging between −30 °C and −35 °C to undergo cell death. Lower temperatures, such as −60 °C, are needed to destroy malignant lesions (Vujewich and Goldberg 2008; Pasqualli 2013). In general, benign conditions require more superficial freezing and, in fact, are better to undertreat a benign lesion than causes an anesthetic hypopigmentation or scar (Fig. 2).

The conductivity of the material interposed between the lesion and the cryogen which determine the final freezing temperatures. Metals are ideal thermal conductors, such as copper (Pasquali et al. 2010).

Thick hyperkeratotic lesions have poor conductivity and should be debridated whenever possible, prior to cryogen application. It is also convenient to debulk nodular lesions or large tumoral masses, to avoid profuse bleeding.

Although there are several hypotheses, the full mechanism of tissue destruction by cryogens remains not completely understood (Petres et al. 1996).

Techniques and Equipment

Over the years, cryosurgical units have evolved from heavy bottles to highly efficient, low-weight, easy-to-use devices. There are storage tanks with 4, 5, 10, 25, 30, 35, and 50 liters of capacity for liquid nitrogen (Pasquali et al. 2010).

There are several techniques to perform cryosurgery. The choice of which should be used depending on the lesion and the operator preference:

- Dipstick technique: The traditional dipping in a cotton-tipped applicator into a cup with liquid nitrogen is generally inadequate, because the freezing is slow and superficial. It is the oldest method (Kuflik and Kuflik 2012). It may be used in small verrucae or similar lesions (Petres et al. 1996).
- Solidified carbon dioxide: A less commonly performed method. A crushed solidified carbon dioxide, contained in a disposable towel, is dipped in acetone and applied lightly onto the lesion, for mild freezing and exfoliation of the skin ("slush therapy") (Kuflik and Kuflik 2012). It can be used for acne vulgaris, acne cysts, rosacea, and flat warts (Kuflik and Kuflik 2012).
- Open spray: The most frequently used. Consists of a handheld cryosurgical unit with a fingertip trigger (Kuflik and Kuflik 2012; Vujewich and Goldberg 2008; Pasqualli 2013). There are different spray tips varying in size. Important factors in determining the amount of cold delivered to the lesion are the tip diameter, intermittent release of the nitrogen, and distance from tip to target (Pasquali et al. 2010). Longer spray times are required for thick and malignant lesions. Shorter times are reserved for benign, thin, and atrophic lesions (Vujewich and Goldberg 2008). Spraying can be delivered in an intermittent or in a continuous manner (Pasqualli 2013). The spray is directed to the lesion from a distance of 1–2 cm (Kuflik and Kuflik 2012). Superficial lesions require a 2–3-mm freeze margin, and malignant and deeper lesions should have a 5-mm margin (Vujewich and Goldberg 2008). The spray devices obtain a temperature of −40 °C to a depth of about 12 mm (Petres et al. 1996).
- Confined spray/closed cone: A variation of the open technique, in which the liquid nitrogen is confined within a cone that is held against the skin. Plastic otoscope cones and specifically designed cones (polycarbonate) can be used.

- Chamber: Another variation of the open technique. The spray is released through an orifice into a metal chamber, firmly held to the lesion. The turbulent movement of the nitrogen inside the chamber lowers the temperature even further. Lower temperatures are achieved faster and require extreme caution. It is usually limited to malignancies (Pasquali et al. 2010).
- Close/cryoprobe/contact: A copper cryoprobe (precooled metal tip) is attached to the cryosurgical unit. The metal probe should be pressed against the lesion on the skin. It is useful for treating small and well-circumscribed lesions or in confined locations (Vujewich and Goldberg 2008).

  The contact freezing achieves −40 °C of temperature but a depth of only about 4 mm (Petres et al. 1996).
- Cryo Tweezers: A variation of the cryoprobe technique, successfully used in pedunculated lesions such as skin tags and warts (Usatine et al. 2015).
- Intralesional: Ideal for voluminous or deep tumors. One or several sterile cannula probes are inserted into one side of the tumor and running it interstitially along the lesion (along the largest axis, at its deepest point) until it appears on the opposite side. Liquid nitrogen is sprayed into the cannula, and an ice cylinder is formed within the center of the lesion. There is minimal surface destruction compared to the previously mentioned techniques (Pasquali et al. 2010).

Preoperative Preparation/Patient Selection

A great advantage for cryosurgery is that it does not require a special surgical area (Pasquali et al. 2010). Therefore it is suitable for patients in wheelchairs or for those who cannot leave their home or nursery. It is a safe technique to patients with underlying medical conditions (heart diseases, bleeding disorders, metabolic diseases).

If there is any suspicion of malignancy, a skin biopsy needs to be performed prior to the cryotherapy procedure. Dermoscopy, ultrasound, radiography, and other imaging tests may be necessary. Once the location, type, and thickness of the lesion are well defined, the surgeon can decide which is the preferable technique to be used. (Pasquali et al. 2010).

Pearls:

- Most lesions do not require previous treatment. In some cases, keratolytic substances, curettage, or debulking may be necessary.
- Irregular surfaces are better treated with the open technique (spray).
- Always work in bloodless areas. Blood increases the local temperature.
- Vascular lesions are better treated with probes, such as hemangiomas and other vascular malformations (see “Laser Treatment of Vascular Lesions”).
- Cartilage and bones are very resistant to freezing.
- Local anesthesia, in most cases, is not required. It may be considered in very anxious patients and children (Pasquali et al. 2010) and in cases of deep freezing (chamber, probe, and intralesional techniques). Topical agents may help and should be applied 30–60 min before the procedure.
- It is very important to inform, verbally and with a consent form, all the expected postoperative course, as possible side effects and probable cosmetic outcome (Pasquali et al. 2010; Pasqualli 2013; Usatine et al. 2015).
- If using probes, be careful not to remove a probe stuck to the surface of the skin. (Pasquali et al. 2010) A small container with warm water may help in case a probe gets stuck to the skin (Pasqualli 2013).
- Fractional cryosurgery may be helpful to avoid deformities and retractile scars in big lesions. It is performed in stages, first in the center of the lesion, reducing its size, and then repeated as necessary until the tumor diameter is smaller than 10 mm, at which the standard procedure is performed (Gonçalves 2009).

Contraindications

- Inexperienced clinicians should avoid this procedure, which can do great harm if used inappropriately (Usatine et al. 2015).
- Despite the lesions, some of them are better dealt with other treatments, such as suspected malignant invasive lesions (melanoma) (Usatine et al. 2015).
- Morpheaform, infiltrative, micronodular, or recurrent basal cell carcinomas are rare, if ever indications for cryosurgery, such as poorly differentiated squamous cell carcinoma. If used, it would only be considered a palliative treatment (Usatine et al. 2015).
- Inappropriate sites: Preauricular and nasolabial folds tend to have high recurrence rates; hair-bearing sites can evolute with permanent hair loss; Fitzpatrick's skin type 4 or 5 patients should be averted about hypopigmentation or hyperpigmentation; lower leg tends to have a bad healing process, especially in patients with poor circulation (Usatine et al. 2015).
- Concurrent diseases that may adversely affect the response to cryotherapy: cold-induced diseases (e.g., cryoglobulinemia, cold urticaria), Raynaud's disease, autoimmune and collagen diseases, platelet deficiency, and pyoderma gangrenosum (Usatine et al. 2015; Zimmerman and Crawford 2012).

Cryotherapy Therapeutic Indications

There are several indications for cryotherapy in the dermatologic field. Above, we list all of them and detail the main and most common in the daily practice.

Benign Lesions (Electrosurgery)

- Acne cysts

  The advent of effective modern medication has decreased the use of cryosurgery to treat inflammatory acne. Some deep nodules may respond to freeze-thaw cycles of 10–20s. Superficial cysts require a single freeze of 5–10s, and the results can be dramatic. There may be temporary crusting. The results can be improved with intralesional triamcinolone (Usatine et al. 2015).
- Acrochordons

  Cryospray with a bent spray tip or a small aperture is a fast and easy method to treat this lesion. Cryo Tweezers is the least painful and efficient technique and especially useful in the eyelids (Usatine et al. 2015).
- Angiofibromas

  Angiofibromas or adenoma sebaceum are cutaneous lesions seen in tuberous sclerosis. Some case reports describe good results with repeated cycles of cryosurgery, but with long freeze times, that may evolute with hypopigmentation. Angiofibromas may be seen as smaller lesions in patients who do not have the syndrome and may respond well to cryospray or contact probe (Usatine et al. 2015).
- Angiomas

  Small vascular lesions such as senile angiomas ("cherry") and spider angiomas may respond to cryosurgery using a cryoprobe, which compresses the lesion during freezing. Ten seconds should be needed. In cases of large angiomas, they may be anesthetized and shaved off, with electrosurgery of the base (Usatine et al. 2015).
- Benign lichenoid keratosis

  Also called lichen planus-like keratosis. Often needs a biopsy to be diagnosed. Once the diagnosis is defined, cryosurgery is an effective treatment option if there is any remaining lesion.
- Chondrodermatitis nodularis helicis

  It is a painful nodule on the pinna, related to mechanic pressure on the ear. It is crucial to be sure that the nodule is not a skin cancer before using a destructive method such as cryotherapy. When clearly benign, it can be frozen with a cryoprobe or spray for 10–20s. Additional treatment includes surgical excision and intralesional steroid injection (Usatine et al. 2015).

- Viral warts/condyloma acuminate

  Cryosurgery remains a standard treatment option to the treatment of viral warts in adults. Young children may not endure the pain (Usatine et al. 2015). The use of local anesthetic cream 1–2 h before therapy may be useful. Human papillomavirus lesions are usually sensitive to cryosurgical procedures and sometimes can be treated in one single session with excellent results (Pasquali et al. 2010).

  As previously mentioned, reduce keratin of verrucae by shaving or using keratolytic substances may improve the results. Wet the area before the freeze cycle to increase cold conductivity.

  In common warts, initially 1–2-mm halo ice should surround the wart and the ice field maintained for 5 s. Filiform warts can be treated with Cryo Tweezers. The maximum results can be achieved with 3 weeks of intervals sessions.

  For the treatment of flat warts, cryosurgery must be carefully considered because there is a high risk of pigmentary changes.
- Dermatofibroma

  Using a freezing method, certainly the nodular component can be flattened, but a pale area may be left behind. Specific studies show that cryospray for at least 30s and a 2 mm border of freeze obtain a good or excellent result (Usatine et al. 2015). Some authors suggest 60s of cycles due to the fibrotic nature of the lesion (Vujewich and Goldberg 2008).
- Digital myxoid cyst

  Cryosurgery is not the gold standard treatment, but if it is chosen, it needs to be aggressive enough to produce fibrosis in the wall of the cyst. Generally it requires two or more freeze-thaw cycles of 30s. Considerable pain and swelling may be present. Draining the viscous fluid before freezing allows a less aggressive 10–20s of cycle (Usatine et al. 2015).
- Granuloma annulare

  The freezing injury may bring a shrinkage or clearing of a plaque, the same as reported with a diagnostic biopsy. When cryosurgery is performed, 5–10-s freeze cycles are recommended to avoid blistering and post-inflammatory hyperpigmentation (Usatine et al. 2015).
- Granuloma faciale

  Cryosurgery has been used as a sole therapy with 10-s freeze cycles, but best results are achieved with following corticosteroid injection.
- Guttate leucoderma

  There is not a gold standard treatment for this lesion. Most of the options have limited improvement rates. Ploysangam et al. reported more than 90.8% success with cryoprobe technique for 10s (Playsangam et al. 1990). Kumarashinghe reported that a 3–5-s cycle is sufficient to achieve repigmentation in idiopathic guttate leucoderma. The exact mechanism of repigmentation is not well defined (Kumarashinghe 2004). It is possible that liquid nitrogen destroys abnormal melanocytes and keratinocytes and permits that surrounding normal melanocytes migrate into the hypopigmented area (Kumarashinghe 2004).
- Hemangiomas

  In newborn babies, a cryoprobe should be firmly applied with a contact interface gel, for 10–20s. Hyperpigmentation and scarring may occur. After the advent of oral and topical beta-blocker for infantile treatment, the use of cryosurgery has fallen out. However, in adults, it remains as a treatment option (Usatine et al. 2015).
- Keloids and hypertrophic scars (see "CO2 laser for scars")

  Cryosurgery is often a good approach but it may fail or need to be repeated several times. There are four approaches for hypertrophic scars and keloids with a cryogen (spray or probe):

  1. Monotherapy: 15-s cycle with 1 mm halo and should be repeated every 4–6 weeks as necessary
  2. Cryosurgery + intralesional corticosteroids: Many studies report a better response rate with this association. Response rate of 86.7%, compared to 70% after cryotherapy alone.
  3. Surgical debulking + contact cryosurgery: Surgical excision, not extending to the

normal skin, followed by a contact cryosurgery of the base of the keloid.

4. Surgical debulking + transfixing cryosurgery: Surgical excision, not extending to the normal skin, followed by transfixing cryosurgery, using a hollow needle, which perforates the base of the keloid, transfixing the lesion. The liquid nitrogen passes through the needle. With this technique the exudate and swelling set up quickly, with less tenderness and less hypopigmentation. It allows shorter intervals between treatments (Usatine et al. 2015).

Recent lesions have an earlier and better response. An Egyptian clinical study showed that a better therapeutic response was achieved after intralesional cryosurgery comparing to contact cryosurgery, with higher flattening rates and fewer side effects (Abdel-Meguid et al. 2015; Weshahy and Abdel 2012). Intralesional therapy also causes minimal damage to the skin surface and less complaints of pain and pruritus (Choudhary et al. 2010; van Leeuwen et al. 2015).

- Lymphangiomas

  Although lymphangiomas may shrink with cryosurgery, the chance of complete resolution is small.

- Molluscum contagiosum

  This is a common viral infection. The number of lesions may vary from one to several hundred and can persist for years (Usatine et al. 2015). Both open and closed techniques can be used (Pasquali et al. 2010). Liquid nitrogen is applied until the lesion becomes white, and the central dimple is highlighted. Point the spray in the center of the lesion, avoiding pendular movements. It is not necessary to freeze beyond the margin of the lesion. If using a probe, it allows the treatment of multiple lesions in a shorter time. There may be temporary swelling, and then shrinkage until the papule falls off.

- Mucocele

  Also called labial mucoid cyst or retention cyst, usually on the lower lip, up to 1 cm. They respond well to cryosurgery but larger lesions should be drained first. Lubricant gel may be applied before the placement of the probe, which is pressed on the lesion for about 10–20s. No lateral spread of ice is necessary (Usatine et al. 2015).

- Pearly penile papules

  Acral angiofibromas often misdiagnosed as warts or sebaceous hyperplasia. Occur after puberty on the corona and sulcus of the glans penis. Cryosurgery is a quick and effective method. Two cycles of 10s with a fine spray are very effective with low morbidity (Usatine et al. 2015).

- Porokeratosis

  No treatment is entirely effective but cryosurgery is often acceptable despite the hypopigmentation. Short freeze of 5–10s with a spray is recommended.

- Pyogenic granulomas

  If there is any doubt, biopsy should be performed. Depending on the size of the lesion, the cycles may range from 15 s to 45 s. Recurrent lesions sometimes require more than one cycle of 20–30s. Higher cure rates are obtained with prior shaving of the lesion, followed by curettage and electrodesiccation.

- Sebaceous hyperplasia

  These lesions not necessarily need treatment, but several therapies are available for aesthetic purpose. If there is any suspicion of BCC, biopsy is mandatory. Cryospray or a tiny probe is placed in the central depression for 5–10s.

- Seborrheic keratosis

  Treatment by cryosurgery is effective, although large and hyperkeratotic lesions are best treated by curettage or shave alone. For lesions with up to few millimeters thick or pedunculated ones, liquid nitrogen can be used. The goal is to produce an ice halo of 2 mm. Treatment times vary widely according to size and thickness but usually range from 10–20s. Curettage after cryospray is also a good option (Pasquali et al. 2010) (Fig. 3).

  Er:YAG laser is also an alternative for the treatment of SKs (Seborrheic Keratosis) in one-step procedure, with better cosmetic results compared to cryotherapy (Gurel and Aral 2015).

  *Dermatosis papulosa nigra is a variant of SK, mainly seen in high Fitzpatrick's phototypes. When treated with cryosurgery, this

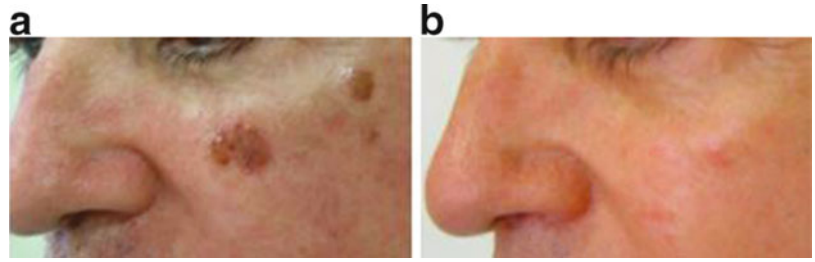

Fig. 3 Seborrheic Keratosis: before (**a**) and after (**b**) 1 session

lesion has a high risk of pigmentary side effects. Light cryosurgery is a better alternative (see "CO2 laser for other indications"; "Fractional Ablative and Non-ablative Lasers for Ethnic Skin").

- Solar lentigo (see "Intense Pulsed Light for Photorejuvenation")

  Most importantly prior to treat any of these lesions, it is to be sure that there are any sign of malignancy (lentigo maligna or lentigo maligna melanoma). If there is any suspicion, a biopsy is the first step.

  For benign lesion, cryosurgery is a quick and effective option. Both spray and cotton-tipped technique is acceptable. The risk of postinflammatory pigment changes exists. Sun protection after the procedure is mandatory. Therefore, a test site in a cosmetically less noticeable region may be performed first before treating multiple lesions. Most of them are superficial, and a single freezing cycle carried out with the spray technique is sufficient to cause a small bulla and sloughing (Vujewich and Goldberg 2008).

  Cryospray can be directed in a zigzag pattern for 1–5 s and should extend 1 mm of the normal skin at the periphery.

  Cryotherapy is considered more effective in achieving substantial skin lightening than TCA but more painful and with longer healing time. Hyperpigmentation is almost equal (Raziee et al. 2008).
- Steatocystoma multiplex

  Although this is not the gold standard treatment, the open spray technique is acceptable as an alternative to surgery. A case report describes a 10-s nitrogen spray cycle with considerable flattening of the cysts after 6 months. (Usatine et al. 2015)
- Syringomas

  Syringomas are purely a cosmetic issue. There are several destructive treatments such as electrodessication, laser, topical TCA, and cryosurgery, all of them with limited success. Cryosurgery may cause swelling around the eyes and hypopigmentation; however, a test may be performed prior to the procedure. Freeze times of 5 s are suggested. Care must be taken to avoid liquid nitrogen in the eye.
- Venous lakes

  Cryoprobe or cryospray may be useful. The advantage of the probe is that it compresses the lake in order to treat the deeper portion of the lesion. Freeze times of 5–15 s with 1–1.5 mm are suggested, according to the size of the lesion.
- Verrucous epidermal naevi

  Hamartomas characterized by epidermal and adnexal structures hyperplasia. Cryosurgery is considered an effective therapeutic modality to treat this condition, with low cost and good cosmetic results.

  Panagiotopoulos et al. described two open spray technique cycles of 10-15 s each, in 12 patients. Ten patients had their naevi successfully treated with no scarring with two to five sessions. One patient showed relapse within 8 months; one patient developed hypochromic scarring (phototype 5), but with repigmentation after 6 months. (Panagiotopoulos et al. 2009).
- Xanthelasma

  Cholesterol-filled yellow plaques usually on the eyelids. They are always benign, and treatment is undertaken for cosmetic reasons.

Cosmetic treatment options include TCA 50–10%, cryosurgery, and surgical excision. Although excision is preferred, cryosurgery may be used but inevitably leads to marked swelling (Simon et al. 2015). When cryotherapy is chosen, the closed probe technique is recommended with 15-s repeated freeze-thaw cycles, depending on the size of the lesion.

Premalignant Lesions

- Actinic keratosis (AK) (see chapter "Photodynamic Therapy" Vol. 1)

  The more affected sites are the back of the hands, forearms, and upper face. There are different morphological varieties: common, pigmented, and cutaneous horn.

  A biopsy should be undertaken in thick lesions with rapid growth, lesions that show any other features of a squamous cell carcinoma (horn, bleeding, pain), pigmented AKs if in melanoma suspicion, and AKs that have failed prior to cryotherapy or other local treatments.

  AKs are most often treated by cryosurgery, with 97% cure rates and 2.1% recurrence in 1 year (Usatine et al. 2015). Freeze times vary from 5s to 10s, with a 1-mm halo, depending on the size and thickness of the lesion. Longer freeze times may evolute with hypopigmentation. (Vujewich and Goldberg 2008; Usatine et al. 2015).

  A European prospective and randomized study compared the efficacy, tolerability, and safety of low-dose 5-FU topical solution (to) cryosurgery in patients with moderate/severe AKs (6 weeks of once daily 5-FU or up to two cryosurgery treatments with 3-week interval). They concluded that 5-FU achieved greater hystological clearance and lower recurrence rates than cryosurgery (Simon et al. 2015).

  Cryopeeling is a modality of treatment that uses diffuse cryotherapy not only in AKs but all over the photodamaged skin. It is an easy-to-perform option, with low cost and reduced healing times, in cases of widespread actinic keratoses. It is highly effective, and the incidence of squamous cell carcinoma is also greatly reduced (Chiarello 2000).
- Actinic cheilitis

  Actinic cheilitis may be treated by cryosurgery using a single 5–10-s freeze-thaw cycle, no margin/halo needed. A second procedure is recommended if the first one was not aggressive enough (3–4-week intervals). If the lesion does not respond to the treatment, a biopsy is needed to avoid SCC.
- Bowen's disease

  Also known as a SCC in situ. There are the common type, the hyperkeratotic type, and the genital type. A biopsy is always recommended to exclude the progression to an invasive malignancy.

  For small and thin lesions, curettage and electrosurgery are appropriate. For small and thicker lesions, excision is the best option. Topical 5-FU 5% and imiquimod 5% cream and PDT can be also considered.

  Cryospray technique can be applied (except in the genital area) with a single 20–30-s freeze cycle with a 2-mm halo including healthy tissue around. Larger lesions can be divided into overlapping circles. Larger lesions may be treated using the spiral or paint-spray technique (20–30s).

  Hyperkeratotic lesions do not respond well to cryosurgery alone and should be debulked priorly.

  For Bowen's disease of the genitalia, a 15–20-s freeze-thaw cycle is recommended and usually has a rapid healing time with good functional and cosmetic results.

  Lesions on the leg, especially in older patients, may have a delayed healing process due to underlying venous stasis, and aggressive cryosurgery may lead to ulceration.

  Recurrence is common if the freeze is not aggressive enough, because the cells migrate back to the surface (recurrence rates range from 5% to 10% if adequate cryosurgery is used).

Postoperative Care and Follow-Up

Postoperative care varies according to the type of the lesion and location and depth of freeze (Kuflik and Kuflik 2012). Patients should be informed about the expected healing time, secondary effects, and complications that may occur, more commonly, erythema, discomfort, or even pain/burning usually (Pasquali et al. 2010).

In superficial freezing, there is no need to cover the lesion; for deep freezing, the wound should be covered with gauze for 48 h, and an antibiotic ointment is optional.[a] In most cases, regular wash with water and soap is sufficient. (Kuflik and Kuflik 2012; Pasqualli 2013) In case of malignancies, there is an extensive exudation process that diminishes as the wound heals. The same procedure of regular washing should be done, but more often (3–4 times/day) in the exudative stage and less often in the granulation phase. A bulla formation is not considered a complication (Kuflik and Kuflik 2012), and it can be drained or not (Pasqualli 2013). Exudation can last a few days to 10–15 days after the procedure. If a crust formation occurs (Fig. 4), the removal can be helpful to speed healing (do not remove crusts of vascular lesions).

In cases of lesions on the legs and ears, and in cases of clinically confirmed secondary bacterial infection (which is rare), some authors recommend oral antibiotic (Kuflik and Kuflik 2012).

An appropriate follow-up after cryosurgery is needed either soon or in long term, to wound check, management of possible side effects, and repeated cycles for same or other lesions if necessary and in cases of recurrent lesions (Usatine et al. 2015).

Fig. 4 Crusts formation after cryotherapy with liquid nitrogen for actinic keratosis treatment on the trunk

Side Effects and Complications

The incidence of complications after cryosurgery is low. It is important to distinguish between what is expected and what is occasional/unusual, temporary, and permanent (Table 1). (Pasquali et al. 2010; Kuflik and Kuflik 2012; Lawrence and Tefler 2010; Vujewich and Goldberg 2008; Petres et al. 1996; Pasqualli 2013; Usatine et al. 2015).

Conclusion

Cryosurgery is considered a versatile treatment option for benign and malignant lesions, with rapid delivery, low cost, and lower morbidity than regular surgery. It is more acceptable in elderly patients with comorbidities and pregnant women. It also has good aesthetic results, and it can be performed either in surgical areas or doctor's offices. Cryotherapy may be used to treat a wide range of skin conditions. The aim of cryosurgery is to promote freezing of the tissue with subzero temperatures, resulting in tissue damage and subsequent healing by second intention. There are several techniques to perform cryosurgery. The choice of which should be used depends on the lesion and the operator preference. Inexperienced clinicians should avoid this procedure, which can do great harm if used inappropriately (Usatine et al. 2015).

Table 1 Expected effects and complications table

Expected
Edema/swelling
Pain
Intradermal hemorrhage
Hypopigmentation
Eschar formation
Vesicle/bulla formation
Exudation
Occasional/unusual/temporary
Secondary infection
Burn
Milia
Headache
Syncope
Hemorrhage of the wound site
Delayed healing
Pyogenic granuloma
Permanent
Hypopigmentation
Achromia
Retraction
Notching of the ala of the nose or ear
Alopecia
Nail dystrophy
Atrophic scar
Hypertrophic scar
Neuropathic pain
Tendon damage
Ectropion
Mucocele on the lip
Erosive pustular eruption on the scalp
Trigger for vitiligo

Take Home Messages

1. Cryotherapy is a useful method in the treatment of multiple lesions.
2. It can be combined with other therapies such as peelings and lasers.
3. It can be used as superficial anesthesia in selected procedures.
4. Cryopeeling can be used to treat a wide cancerization field.
5. Good cosmetic and therapeutic outcome for actinic keratoses.

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